DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-039/S-005

Glaxo Wellcome Inc.
Attention: Robert Watson
Director, Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Watson:

Please refer to your Supplemental Application: Labeling, dated April 7, 2000, received April 10, 2000 for Agenerase™ (amprenavir) Oral Solution submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act.

Please also refer to our February 9, 2000 letter requesting that the Agenerase™ labeling be revised to include a warning about the potential for significant interactions between St John's Wort and antiviral drugs metabolized by the cytochrome P450 system.

This supplemental new drug application provides for the addition of the recommendation that St. John's Wort and Agenerase not be coadministered. Specifically:

WARNINGS

Concomitant use of AGENERASE and St. John's wort (hypericum perforatum) or products containing St. John's wort is not recommended. Coadministration of protease inhibitors, including AGENERASE, with St. John's wort is expected to substantially decrease protease inhibitor concentrations and may result in suboptimal levels of amprenavir and lead to loss of virologic response and possible resistance to AGENERASE or to the class of protease inhibitors.

PRECAUTIONS: Information for Patients

AGENERASE may interact with some drugs; therefore, patients should be advised to report to their doctor the use of any other prescription, nonprescription medication, or herbal products, particularly St. John's wort.

Patient Package Insert:

Taking AGENERASE with St. John's Wort (hypericum perforatum, a nonprescription herbal product) or products containing St. John's Wort is <u>not</u> recommended. Talk with your doctor if you are taking or are planning to take St. John's Wort because St. John's Wort may reduce the effect of AGENERASE.

We have completed the review of this supplemental new drug application and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective as recommended in draft labeling text dated December 8, 2000. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (text for the package insert and text for the patient package insert dated December 8, 2000.)

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten copies on heavy weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format-NDAs* (January 1999). For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved supplement NDA 21-039 (S-005). Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have questions, please contact Melissa M. Truffa, R.Ph., Regulatory Project Manager, at (301) 827-2335.

Sincerely yours,

Debra Birnkrant, M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research